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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/734,644	12/15/2003	Jay Bua	029488-0112	9030

22428 7590 08/23/2005

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EXAMINER	
FETTEROLF, BRANDON J	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 08/23/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/734,644	BUA, JAY	
	Examiner	Art Unit	
	Brandon J. Fetterolf, PhD	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *See Continuation Sheet*.

Continuation of Attachment(s) 6). Other: printout from breast cancer.org.

Jay Bua

DETAILED ACTION

Current Application Status

Claims 1-12 are currently pending and under consideration.

Information Disclosure Statement

The Information Disclosure Statement filed 10/05/2004 and 04/06/2005 are acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner. A signed copy of the IDS is attached hereto.

The information disclosure statement filed on 06/17/2004 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because reference A7 does not appear to be present. It has been placed in the application file, but the information referred to therein has not been considered as to the merits. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609 ¶ C(1).

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-12 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: (a) what is being treated; and (b) what is the result, i.e. outcome, of administering 4-hydroxy tamoxifen percutaneously to a patient having dense breast tissue. In the instant case, it is unclear whether the amount of dense breast tissue is reduced or increased.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-12 are rejected under 35 U.S.C. 102(b) as being anticipated by Mauvaris-Jarvis et al. (U.S. 4,919,937, 1990).

Mauvaris-Jarvis et al. teach (column 4, lines 46-53) a method of treating conditions of the breast comprising administering percutaneously an aqueous alcoholic gel comprising trans-4-hydroxy tamoxifen. With regards to the aqueous alcoholic gel, the patent teaches that the alcoholic gel enables percutaneous penetration to take place, wherein the gel comprises Carbopol ®, ethyl alcohol or water. With regards to the conditions of the breast treated, Mauvaris-Jarvis et al. teach that the conditions of the breast include benign cancerous affections (abstract). The patent further teaches that the formulation of the gel comprises 0.15g of 4-hydroxytamoxifen (column 3, line 33). Thus, while Mauvaris-Jarvis *et al.* does not characterize the patient as having dense breast tissue, wherein the tissue is dense or nodular, the claimed functional limitation would be an inherent property of the referenced method because as evidenced by Brisson et al. (Cancer Epidemiology, Biomarkers & Prevention 2000; 9: 911-915, IDS), extensive breast densities have been related to histological characteristics of breast tissue, such as epithelial hyperplasia (with or without atypia), carcinoma in situ, and stromal fibrosis (page 913, 2nd column, last paragraph). Thus, while the reference does not explicitly state that the breast tissue is diffuse or nodular, it does not appear that

the claim language or limitation results in a manipulative difference in the method steps when compared to the prior art disclosure. See Bristol-Myers Squibb Company v. Ben Venue Laboratories 58 USPQ2d 1508 (CAFC 2001). Granting a patent on the discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art. In re Baxter Travenol Labs, 21 USPQ2d 1281 (Fed. Cir. 1991). See M.P.E.P. 2145. Furthermore, although Mauvaris-Jarvis et al. does not teach that the 4-hyroxy tamoxifen administered is a racemic mixture of both trans and cis isomer, the claimed limitation would be an inherent property of the percutaneous administration of trans-4-hydroxy tamoxifen because as evidenced by Mauvais-Jarvis (Cancer Research 1986; 46: 1521-1525, IDS), percutaneous administration of the trans-4-OHTAM resulted in an equal yield of the cis and trans isomers of 4-OHTAM from breast tissue (page 1522, 2nd column, 6th paragraph). Thus, it does not the claimed limitation results in a manipulative difference in the products used when compared to the prior arts disclosure. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

Claims 1-12 are rejected under 35 U.S.C. 102(b) as being anticipated by Pujol et al. (Cancer Chemother. Pharmacol 1995; 36: 493-498).

Pujol et al. teach a method of administering 4-hydroxy tamoxifen percutaneously to patients with normal breast tissue and patients with breast cancer (Title). With regards to the percutaneous route, the reference teaches 4-hydroxy tamoxifen was formulated in a hydroalcoholic gel and applied at a dose of 0.5 mg/day or 1 mg/day to both breasts (page 494, 1st column, paragraphs 4 and 5). Thus, while Pujol et al. does not characterize the patient as having dense breast tissue, wherein the tissue is diffuse or nodular, the claimed functional limitation would be an inherent property of the patients suffering from breast cancer because as evidenced by breastcancer.org (see attached), breast cancer itself is made up of dense tissue. Thus, it does not appear that the claim language or

limitation results in a manipulative difference in the method steps when compared to the prior art disclosure. See Bristol-Myers Squibb Company v. Ben Venue Laboratories 58 USPQ2d 1508 (CAFC 2001). Furthermore, while Pujol et al. does not teach that 4-hydroxy tamoxifen is in a vehicle containing a penetration enhancer, the claimed functional limitation would be an inherent property of the referenced hydroalcoholic gel since the specification teaches (page 9, paragraph 0032) that enhancers include alcohols. Thus, there does not appear to be a structural difference between the hydroalcoholic gel and the instantly claimed vehicle containing a penetration enhancer. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989). Moreover, while Pujol et al. does not teach that the 4-hyroxy tamoxifen administered is all trans 4-hydroxy tamoxifen or a racemic mixture of both trans and cis isomers, the claimed limitation would be an inherent property of the percutaneous administration of trans-4-hydroxy tamoxifen because as evidenced by Mauvais-Jarvis (Cancer Research 1986; 46: 1521-1525, IDS), percutaneous administration of the trans-4-OHTAM resulted in an equal yield of the cis and trans isomers of 4-OHTAM from breast tissue (page 1522, 2nd column, 6th paragraph)

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-12 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-12 of copending Application No. 10/734638.

Although the conflicting claims are not identical, they are not patentably distinct from each other. In the instant case, the method of treatment, comprising administering 4-hydroxy tamoxifen to a patient having breast cancer claimed in the conflicting application appears to fall within the same scope of a method of treatment comprising administering 4-hydroxy tamoxifen to a patient having dense breast tissue claimed in the application being examined, and therefore, a patent to the method of treatment, wherein the patient has breast cancer would necessarily, extend the rights of a method of treatment, wherein a subject has dense breast tissue should the application being examined issue as a patent after the conflicting application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Furthermore, Claims 1-12 are provisionally rejected under 35 U.S.C. 103(a) as being obvious over copending Application No. 10/734638 which has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the copending application, it would constitute prior art under 35 U.S.C. 102(e) if published or patented. This provisional rejection under 35 U.S.C. 103(a) is based upon a presumption of future publication or patenting of the conflicting application.

This provisional rejection might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the copending application was derived from the inventor of this application and is thus not the invention "by another," or by a showing of a date of invention for the instant application prior to the effective U.S. filing date of the copending application under 37 CFR 1.131. This rejection might also be overcome by showing that the copending application is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

Therefore, NO claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brandon J. Fetterolf, PhD whose telephone number is (571)-272-2919. The examiner can normally be reached on Monday through Friday from 8:30 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeff Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Brandon J Fetterolf, PhD
Examiner
Art Unit 1642

BF

JEFFREY SIEW
SUPERVISORY PATENT EXAMINER
8/14/05

breastcancer.org

<< High Breast Density a Risk Factor

High Breast Density, A Risk Factor for Breast Cancer, May Be Largely Inherited

New England Journal of Medicine, September 19, 2002

Other Articles in this Edition
Breast Self Exams May Not Reduce Breast Cancer Deaths

Hair Dye and Breast Cancer Risk

Low-Fat Dairy Food May Help Protect Pre-menopausal Women

Background and importance of the study: Past research has shown that women with "dense" breasts are more likely to be diagnosed with breast cancer than women whose breasts are less "dense." Dense breasts contain more glandular and connective tissue. Less dense breasts are mainly made up of fat tissue. Every woman has different amounts of the different types of tissue in her breasts.

Breast cancer itself is made up of dense tissue. This means that, on a mammogram, a tumor is harder to spot in dense tissue than in fatty tissue, because the tumor looks a lot like the tissue around it. So one possible explanation for the higher rate of breast cancer in women with dense breasts is that mammograms are less likely to find tumors early in those women.

But researchers don't believe this is the whole story. Past research suggests some type of link between dense breasts and a higher risk for breast cancer.

Words on this page
• mammogram
• menopausal
• gene
• tumor
• hormone replacement therapy
• ultrasound
• MRI

The link isn't a direct, cause-and-effect connection: Just because a breast is dense doesn't mean it's more likely to have cancer develop in it. Instead, researchers believe that breast density and breast cancer risk may BOTH be affected by the same inherited genes. To prove this, researchers first have to be sure that both breast cancer risk and breast density are in fact affected by inheritance (genetics).

Breast cancer risk is already known to be at least partly inherited.

We know that you have a higher risk if other people in your family have been affected by the disease.

But what about breast density? Previous studies have shown that age, menopausal status, weight, and number of children account for just 20% to 30% of the variation in breast density among women.

In order to determine how much of the REMAINING variation in breast density is due to inherited, or genetic, factors, researchers decided to study groups of twins.

Twins are good study subjects because they share genetic backgrounds and usually—at least during childhood—live in the same environment. Identical twins have exactly the same genes, while fraternal twins share only some of their genes. By comparing groups of identical and fraternal twins, researchers can look at how much certain traits are affected by genes and how much they're affected by environment.

For example, if pairs of identical twins who grew up in the same household have very similar musical abilities, while fraternal twins who grew up in the same household have very different musical abilities, researchers might conclude that genes have a stronger effect than environmental factors on musical ability.

Study design: Researchers studied four groups of identical and fraternal female twins from Australia, Canada, and the United States:

- 353 pairs of identical twins and 246 pairs of fraternal twins from Australia
- 218 pairs of identical twins and 134 pairs of fraternal twins from Canada and the United States

The women in the study were between the ages of 40 and 70, had either undergone or were willing to undergo mammography, and did NOT have breast cancer.

In addition to studying the women's mammograms, researchers asked all of the twins to complete questionnaires about their:

- weight
- height

- exercise patterns
- smoking history
- alcohol consumption patterns
- menstrual and reproductive histories
- use of oral contraceptives and hormone replacement therapy.

The women were also asked whether they had a family history of cancer.

Results: These studies of twins provided strong evidence that the variation in breast tissue density seen on mammograms is strongly influenced by genetic factors.

First researchers took into account how old the women were and other non-genetic factors known to influence breast density, such as the number of children they'd given birth to and menopausal status. After these factors were considered, identical twins were more than TWICE as likely as fraternal twins to have similar levels of breast density.

Researchers also looked at breast density in women with and without close relatives affected by breast cancer. Of the women in the study, 11% (112 pairs of twins) had at least one close female relative with breast cancer. And women in this group had denser breasts than women who had no close relatives with the disease.

Conclusion: This study suggests that breast density may be more influenced by the genes you inherit than by any particular thing you do during your lifetime, such as what you eat, how much you exercise, or how many children you have.

Knowing this, researchers can look for the specific genes that affect breast density. And because there seems to be a connection between high breast density and an increased risk for breast cancer, the same genes might also play a role in that risk.

Take-home message: Genes you inherit from your parents probably have a bigger influence on the density of breast tissue, as determined by mammography, than any other single factor. Knowing this is important mainly for researchers who are looking

for the underlying genetic factors affecting breast cancer.

For women it's important to know that increased breast density, as shown on a mammogram, may be associated with a higher risk of breast cancer. If this is the case, then it's important to understand the best way for doctors to follow women with dense breasts. For example, can ultrasound or MRI scanning add valuable information beyond a simple mammogram?

If your mammogram reveals dense breasts—particularly if you have other factors that might put you at an increased risk for breast cancer—ask your doctor if any additional tests would be appropriate to give a clearer picture.

breastcancer.org
PO Box 222 Narberth, PA 19072-0222
Contact Us